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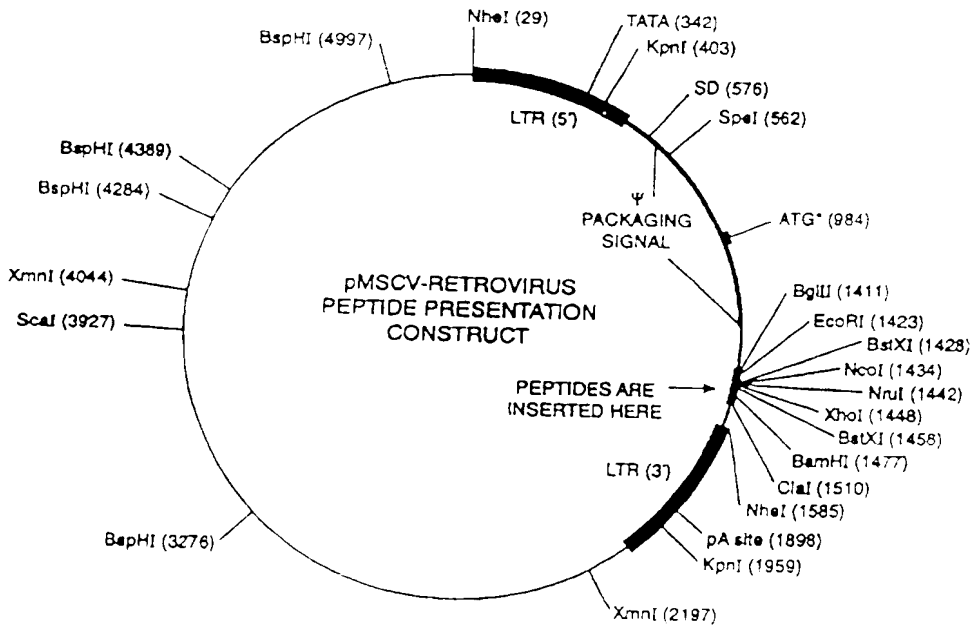

(57) Abstract

Methods and compositions for screening for intracellular transdominant effector peptides and RNA molecules selected inside livin cells from randomized pools are provided.

CLAIMS

I claim:

1. A method for screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:
a) introducing a molecular library of randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence;
b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent.

2 A method according to claim 1 further comprising the step:
c) isolating said cell exhibiting an altered phenotype.

3 A method according to claim 2 further comprising the step:
d) isolating a candidate nucleic acid from said cell.

4. A method according to claim 2 or 3 further comprising the step:
e) isolating a target molecule using
i) a candidate nucleic acid; or
ii) the expression product of a candidate nucleic acid.

5. A method according to claim 1 wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized candidate expression products.

6. A method according to claim 5 wherein said randomized candidate expression products are peptides.

7. A method according to claim 5 wherein said randomized candidate expression products are nucleic acid transcripts.

8. A method according to claim 1 wherein said nucleic acids further comprise a presentation sequence capable of presenting said expression product in a conformationally restricted form.

9. A method according to claim 1 wherein said introducing is with retroviral vectors.

10. A method according to claim 1 wherein said cells are mammalian cells.

11. A method according to claim 1 wherein said library comprises at least 10^4 different nucleic acids.

12. A method according to claim 1 wherein said library comprises at least 10^5 different nucleic acids.

13. A method according to claim 1 wherein said library comprises at least 10^6 different nucleic acids.

14. A method according to claim 1 wherein said library comprises at least 10^7 different nucleic acids.

15. A method according to claim 1 wherein said library comprises at least 10^8 different nucleic acids.

16. A molecular library of retroviruses comprising at least 10^4 different randomized nucleic acids.

17. A molecular library of retroviruses according to claim 21 comprising at least 10^5 different randomized nucleic acids.

18. A molecular library of retroviruses according to claim 21 comprising at least 10^6 different randomized nucleic acids.

19. A molecular library of retroviruses according to claim 21 comprising at least 10^7 different randomized nucleic acids.

20. A molecular library of retroviruses according to claim 21 comprising at least 10^8 different randomized nucleic acids.

21. A cellular library of mammalian cells containing a molecular library of retroviral constructs, said molecular library comprising at least 10^4 different randomized nucleic acids.

22. A cellular library according to claim 26 wherein said constructs are integrated into the cellular genome.